

# The patient who 'spilled salt'

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## How would you handle this case?

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Mrs. V has psychotic depression and hyponatremia. Is beer drinking or diuretic use causing her low serum sodium? Or could it be something else?

### HISTORY 'They're out to get me'

Mrs. V, age 64, tells her primary care physician she has felt "bad" for 2 weeks. She complains of depressed mood, middle insomnia, diminished appetite, poor concentration, and poor energy. She denies suicidal thoughts but reports feeling alone, overwhelmed, and unable to manage her daily life.

Mrs. V is very concerned about losing her job because she cannot function at work. She believes her coworkers may be plotting to get her fired. The primary care physician refers Mrs. V to us to evaluate her mood.

According to her daughter, Mrs. V has had multiple psychiatric hospitalizations; the most recent occurred 2 years ago when she was admitted for paranoia and disorganized behavior. The daughter also mentions that her mother has a remote history of daily alcohol use, drinking until she was intoxicated. Mrs. V says she occasionally drinks beer and she scores 2 out of 4 on the CAGE questionnaire, which may indicate alcohol dependence.

During mental status examination, Mrs. V is alert and oriented to person, place, and date. She is pleasant and cooperative but shows apparent thought blocking and some tangentiality. She has substantial difficulty

answering questions and articulating symptoms. Speech is slow in rate and rhythm. Mrs. V's mood is severely depressed and her affect constricted.

She denies suicidal or homicidal ideations or visual or auditory hallucinations. Cognitive testing reveals mild deficits in recall memory and poor concentration. Her insight is limited and her judgment fair.

Her medical history includes hypertension, hyperlipidemia, coronary artery disease, cardiac catheterization, and hyponatremia. Her medication regimen consists of aripiprazole, 15 mg/d; diltiazem, 180 mg/d; atenolol, 25 mg/d; aspirin, 325 mg/d; atorvastatin, 10 mg/d; sertraline, 50 mg/d; and ibuprofen, 600 mg as needed for hip pain. She also reports taking diuretics in the past.

Vital signs include blood pressure, 125/95 mm Hg; respirations, 16/min; temperature, 98.2° F; and pulse rate, 72/min. Serum investigations reveal sodium, 119 mEq/L (normal range: 135 to 145 mEq/L) and random blood sugar, 160 mg/dL (normal range: 60 to 114 mg/dL).

### Which test would you order next?

- serum osmolality
- urine osmolality
- urine sodium levels
- serum thyroid-stimulating hormone (TSH) and free thyroxine levels
- serum cortisol levels or adrenocorticotropic hormone (ACTH) stimulation test

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### The authors' observations

The combination of major depression with psychosis and hyponatremia makes Mrs. V's case challenging. Hyponatremia in psychiatric inpatients can prompt medical consultation, thus possibly halting or delaying psychiatric treatment.

Hyponatremia has been associated with the use of:

- diuretics
- selective serotonin reuptake inhibitors (SSRIs)
- serotonin-norepinephrine reuptake inhibitors (SNRIs)
- tricyclic antidepressants
- calcium antagonists.

Elevated creatinine levels, chronic obstructive pulmonary disease, hypertension, systolic blood pressure, and diabetes also can lead to hyponatremia.

Among psychiatric inpatients, the risk of hyponatremia is doubled in women.<sup>1</sup> It is unclear, however, if female gender is an independent risk factor for hyponatremia. Sharabi et al<sup>2</sup> reported that patients of both sexes age >65 have a 9-fold greater risk of developing hyponatremia than younger counterparts.

In addition, hyponatremia risk during any antidepressant treatment is highest:

- in the summer
- during the first weeks of treatment
- with concomitant drug use, especially with diuretics.<sup>3</sup>

### What is the most likely cause of Mrs. V's hyponatremia?

- a) syndrome of inappropriate antidiuretic hormone (SIADH)
- b) congestive heart failure
- c) consumption of large quantities of beer or use of recreational drugs
- d) psychogenic polydipsia
- e) uncorrected hypothyroidism or cortisol deficiency (adrenal insufficiency, hypopituitarism)
- f) nephrotic syndrome
- g) hyperglycemia

continued

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\*Data compiled from a study comparing the young adult adaptive outcome of nearly 140 patients (ADHD and non-ADHD control) followed concurrently for at least 13 years.

Reference: 1. Barkley RA, Fischer M, Smallish L, Fletcher K. Young adult outcome of hyperactive children: adaptive functioning in major life activities. *J Am Acad Child Adolesc Psychiatry*. 2006;45:192-202.

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### Clinical Point

SSRI use in elderly persons has been associated with hyponatremia

**Table 1**

### Mrs. V's laboratory results

	Normal range	Mrs. V's results	
		Before Tx	After Tx
Serum sodium (mEq/L)	135 to 145	119	127
Serum potassium (mEq/L)	3.5 to 5.0	3.6	3.8
Creatinine (mg/dL)	0.5 to 1.7	0.74	0.84
Glucose (mg/dL)	60 to 114	160	150
<b>Osmolarity</b>			
Serum (measured; mOsm/L)	275 to 300	258	242
Urine (mOsm/L)	<150	257	180
Urine sodium (mEq/L)	20 to 40	48	42

#### The authors' observations

To identify the cause of Mrs. V's hyponatremia, we determine her volume status and measure serum osmolality.<sup>4</sup> Next, we measure urinary sodium and osmolality and assess her extracellular fluid status. We also evaluate her renal and adrenal function, which were within normal limits. Although Mrs. V reports fatigue and weakness, there is no evidence of dehydration.

Based on Mrs. V's initial lab results (Table 1), we classify her hyponatremia as euvolemic, with high urine osmolality ( $\geq 100$  mOsm/L). That helps narrow our differential diagnosis to glucocorticoid deficiency, hypothyroidism, and SIADH (Table 2, page 102).<sup>5</sup> We exclude psychogenic polydipsia, "tea and toast" syndrome, or beer potomania because they usually present as euvolemic hyponatremia with low urinary osmolality.

SSRI use in elderly persons has been associated with hyponatremia, which in some cases may be consistent with SIADH.

Unfortunately, few psychiatrists are aware of this potentially fatal side effect.

SIADH occurs in association with reduced serum osmolality. It is characterized by:

- hypotonic hyponatremia (serum sodium  $< 130$  mEq/L)
- inappropriately elevated urine osmolality ( $> 200$  mOsm/L) relative to plasma osmolality
- elevated urine sodium (typically  $> 20$  mEq/L).<sup>4</sup>

We diagnose Mrs. V with SIADH because she has these lab findings in the absence of diuretic therapy; in the presence of euvolemia without edema; and in the setting of otherwise normal cardiac, renal, adrenal, hepatic, and thyroid function.

The key to the pathophysiology, signs, symptoms, and treatment of SIADH is understanding that the hyponatremia is a result of excess water and not a sodium deficiency. Hyponatremia's signs and symptoms primarily are related to CNS dysfunction and correlate with how rapidly and severely the condition develops.

We monitor Mrs. V for anorexia, nausea, and malaise because they would be the earliest findings, followed by headache, irritability, confusion, muscle cramps, weakness, obtundation, seizures, and coma. These occur as osmotic fluid shifts and results in cerebral edema and increased



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intracranial pressure. When sodium concentration drops below 105 mEq/L, life-threatening complications are likely.

**What is the most likely cause of Mrs. V's SIADH?**

- a) CNS disease—tumor, trauma, infection, delirium tremens
- b) pulmonary disease—tumor, pneumonia, chronic obstructive pulmonary disease
- c) carcinoma
- d) medications—SSRIs

**SSRIs and SIADH**

Bouman et al<sup>6</sup> estimated that the incidence of SSRI-induced SIADH in elderly patients is 12%. Liu et al<sup>7</sup> described 706 cases of hyponatremia associated with SSRI use in unpublished reports. Fluoxetine was most commonly the cause (75.3% cases), followed by paroxetine (12.4%), sertraline (11.7%), and fluvoxamine (1.5%). Resuming the same drug resulted in hyponatremia in 16 of 24 of these cases (66.7%).

Kirby et al,<sup>8</sup> however, found no clear advantages in different SSRIs' propensity to cause hyponatremia. Seventy-one percent of patients treated with the SNRI venlafaxine developed hyponatremia, compared with 32% taking paroxetine and 29% receiving sertraline. It is unclear whether a specific SSRI or venlafaxine has a stronger association with hyponatremia than any other antidepressant.

Hyponatremia's nonspecific symptoms and wide range of time to detection (1 to 253 days) suggest clinicians usually detect the condition by chance rather than specifically assessing for it.<sup>9</sup>

**TREATMENT Medication change?**

Coordinating Mrs. V's depression and hyponatremia treatment is critical. We propose discontinuing sertraline and treating Mrs. V's symptoms with electroconvulsive therapy (ECT). She refuses ECT, stating "I don't feel that bad. My father was treated with ECT and I am scared of it."

continued

# IMPACTFUL FACTS

Adults with ADHD were **2X** more likely to have been involved in 3 or more car crashes\*<sup>1</sup>

**The consequences may be serious.  
Screen for ADHD.**

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[www.consequencesofadhd.com](http://www.consequencesofadhd.com)  
and download patient support materials,  
coupons, and adult screening tools.

\*Data from a study comparing driving in 105 young adults with ADHD to 64 community control adults without the disorder.

**Reference:** 1. Barkley RA, Murphy KR, DuPaul GJ, Bush T. Driving in young adults with attention deficit hyperactivity disorder: knowledge, performance, adverse outcomes, and the role of executive functioning. *J Int Neuropsychol Soc.* 2002;8:655-672.



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Table 2

## Hyponatremia: Differential diagnosis

Hypovolemic hyponatremia	Euvolemic hyponatremia	Hypervolemic hyponatremia
Vomiting Diarrhea Laxative abuse Renal disease Nasogastric suction Salt-wasting nephropathy Addison's disease	Normal urinary sodium Glucocorticoid deficiency Hypothyroidism Certain drugs SIADH  Low urinary osmolality Psychogenic polydipsia 'Tea and toast' syndrome Beer potomania	Congestive heart failure Nephrotic syndrome Cirrhosis

SIADH: syndrome of inappropriate antidiuretic hormone  
Source: Reference 5

## Clinical Point

To treat SSRI-induced hyponatremia, consider switching the patient to an antidepressant from a different class and restrict fluid intake

We decide to switch to mirtazapine, a tetracyclic antidepressant. In a case report mirtazapine was successfully used in a similar patient.<sup>10</sup> We continue to monitor Mrs. V's serum sodium concentrations and emphasize the importance of complying with fluid restrictions, instructing her to limit her fluid intake to 250 to 500 mL (1 to 2 glasses) per day.

## The authors' observations

SSRI-induced hyponatremia can be transient or persistent and recurrent. The usual approach is to discontinue the SSRI and try a different antidepressant. Because hyponatremia has been associated with all SSRIs and SNRIs, it would be prudent to choose an alternate antidepressant agent outside these classes. If patients must continue taking an antidepressant that causes hyponatremia, avoid concurrent use of drugs that cause hyponatremia, restrict fluid intake, and consider adding a medication that prevents hyponatremia, such as demeclocycline or fludrocortisone.

SSRI-induced hyponatremia may resolve:

- with SSRI discontinuation alone<sup>11</sup>
- with fluid restriction and without discontinuation of the SSRI<sup>11</sup>
- with drug discontinuation, fluid restriction, and sodium chloride and potassium supplementation.<sup>12</sup>

## FOLLOW-UP Analysis error?

Despite modifications to Mrs. V's diet, her fasting serum glucose level remains >100. She is diagnosed with diabetes mellitus type 2 and treated with metformin. We continue mirtazapine, which has successfully controlled Mrs. V's depressive symptoms. Her serum sodium levels start normalizing.

## The authors' observations

In patients with serum hyperglycemia—such as Mrs. V—correct laboratory analysis yields low serum sodium levels, but these levels do not reflect a true hypo-osmotic state. Accumulation of extracellular glucose induces a shift of free water from the intracellular space to the extracellular space. For each 100 mg/dL increase above normal serum glucose concentration, serum sodium concentration is diluted by a factor of 1.6 mEq/L. Systemic osmolality is normal or increased, but not decreased as would be the case in true (hypo-osmotic) hyponatremia.

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## Related Resources

• Siegel AJ. Hyponatremia in psychiatric patients: update on evaluation and management. *Harv Rev Psychiatry* 2008;16(1):13-24.

• Atalay A, Turhan N, Aki OE. A challenging case of syndrome of inappropriate secretion of antidiuretic hormone in an elderly patient secondary to quetiapine. *South Med J* 2007;100(8):832-3.

### Drug Brand Names

Aripiprazole • Abilify	Ibuprofen • Advil, Motrin, others
Atenolol • Tenormin	Metformin • Glucophage, Diabex, others
Atorvastatin • Lipitor	Mirtazapine • Remeron
Demeclocycline • Declomycin, Declostat, others	Paroxetine • Paxil
Diltiazem • Cardizem, Dilacor, others	Sertraline • Zoloft
Fludrocortisone • Florinef	Venlafaxine • Effexor
Fluvoxamine • Luvox	

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## Clinical Point

**In patients with serum hyperglycemia, low serum sodium levels do not reflect a true hypo-osmotic state**

## Bottom Line

SIADH-induced hyponatremia is a serious, underestimated complication of selective serotonin reuptake inhibitor (SSRI) use that in elderly patients usually occurs within the first month of treatment. When prescribing an SSRI, monitor serum sodium concentrations in older persons and patients with nonspecific symptoms that occur in conjunction with SSRI treatment. Because replacing one SSRI with another will not necessarily prevent hyponatremia from recurring, consider switching to an antidepressant from a different class.